



Case Report

Lemierre syndrome and unexpected death in childhood

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ABSTRACT

Lemierre syndrome refers to necrotizing infections of the head due to *Fusobacterium necrophorum* and has been called the 'forgotten disease' due to its rarity in the antibiotic era. Recently, however, more cases have been documented in the literature suggesting that there has been an increase in incidence. A 10-year-old boy is reported who had a five-day history of ear infection, with the development of fever, drowsiness and ipsilateral neck swelling. Unexpected cardiac arrest occurred soon after medical assessment. At autopsy, right otitis media was demonstrated with extension of suppurative infection into subcutaneous tissues behind the ear and also into the extradural space at the lateral end of the petrous temporal bone. There was also septic thrombophlebitis of the adjacent sigmoid sinus, but no evidence of meningitis. This case demonstrates yet another infectious condition that may be associated with rapid deterioration and unexpected death in childhood. An autopsy approach to suspected sepsis in childhood is outlined.

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1. Introduction

In 1936 Lemierre reported 18 lethal cases of sepsis due to an anaerobic bacteria *Bacillus funduliformis*, now known as *Fusobacterium necrophorum*. There were also two survivors in this series. Lemierre identified six subgroups, including those with the primary infection within the nasopharynx (most often the tonsils and adjacent tissues and called by Lemierre 'anaerobic postanginal septicaemias'), the mouth and jaws, the ear or mastoid, the post-partum uterus; the appendix, and the urinary tract.¹ The term Lemierre syndrome is now most often used for cases of necrobacillosis due to *F. necrophorum* sepsis that are restricted to the head, corresponding to Lemierre's initial three subgroups,² however other types of organisms are occasionally reported.³

As cases of Lemierre syndrome were rare in the 1960s and 1970s, attributed to the effects of antibiotic treatment of pharyngeal infections, it has been referred to as the 'forgotten disease'.^{4–6} While increasing numbers of cases are now being reported, thought to be due to reduced antibiotic usage for pharyngeal infections or to the development of antibiotic resistance,^{7,8} they are still uncommon with an incidence of approximately only one case (0.8) per million being reported in a Danish study from 1990 to 1995.⁹ Although it has also been suggested that another

reason or the apparent increase in numbers of case may have been due to improved anaerobic blood culture techniques,⁷ other studies have not shown a relationship in numbers of cases reported to changes in microbiological techniques.¹⁰ The following report details the pathological features of a case involving a 10-year-old boy and demonstrates that Lemierre syndrome may be a cause of unexpected death in the young.

2. Case report

A 10-year-old boy with a history of right ear pain for three days with loss of appetite and balance was taken to his general practitioner. He had been previously well with a history of stable asthma and attention deficit disorder. At the clinic he was noted to be drowsy and febrile, with swelling and pain of the right side of his neck, and bleeding from the right ear. A diagnosis of bilateral ear infections with an upper respiratory infection was made, along with a recommendation for hospital assessment and treatment. Despite this advice he was taken home with prescribed oral amoxicillin, clavulanate and paracetamol, where he developed respiratory distress and collapsed 20 min after his first dose of antibiotic syrup. Ambulance officers found him in asystole. Sinus rhythm was eventually restored in hospital however resuscitative attempts eventually failed, with death occurring 4.5 h after his initial presentation. The clinical impression was either of death due to sepsis complicating right otitis media or to an anaphylactic reaction to amoxicillin.

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An autopsy performed three days later confirmed right otitis media with extension of suppurative infection into subcutaneous tissues behind the ear and into the extradural space at the lateral end of the petrous temporal bone (Fig. 1). Pleomorphic gram-negative filamentous bacteria were identified on microscopy. There was also septic thrombophlebitis of adjacent veins (Fig. 2) and marked reactive enlargement of cervical lymph nodes. The lungs showed marked congestion and edema. There was no evidence of meningitis or of any primary or metastatic infectious loci in other organs. There was no histologic evidence of asthma. No other underlying organic diseases that could have caused or contributed to death were present, and there was no evidence of trauma. Microbiological studies revealed pure growths of *F. necrophorum* in swabs from the right middle ear and from subcutaneous pus behind the ear. The results of antemortem blood cultures taken in hospital also subsequently revealed *F. necrophorum*. Toxicological tests were unremarkable, serum tryptase was normal and there were no specific IgE antibodies to amoxicillin. Death was, therefore, due to *F. necrophorum* sepsis in Lemierre syndrome, with no evidence of anaphylaxis.



Fig. 1. Inner aspect of the petrous temporal bone showing pus in the extradural space in continuity with infectious material in the middle ear and adjacent soft tissues of a 12-year-old boy who died of fulminant *Fusobacterium necrophorum* infection.

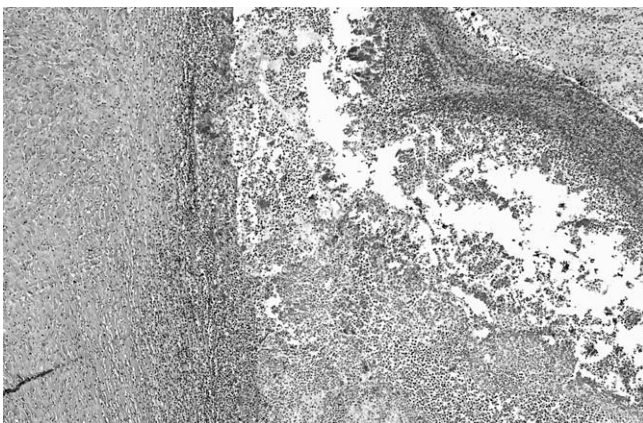


Fig. 2. Septic thrombophlebitis in a vein adjacent to the ear of a 12-year-old boy with *Fusobacterium necrophorum* infection showing a transmurular acute inflammatory infiltrate with superimposed thrombosis (Hematoxylin & eosin $\times 110$).

3. Discussion

Sudden natural death in children is a rare event and infectious causes of unexpected childhood death are even less common. The most frequent situations in developed countries involve pneumonia, gastroenteritis, myocarditis or meningococcal meningitis/septicemia.^{11,12} Deaths from upper airway compromise due to acute epiglottitis caused by *Hemophilus influenzae* are rarely seen nowadays following successful vaccination campaigns in the 1990s, although airway compromise may occur from other types of oropharyngeal infections.¹³ Rare infectious causes of sudden death in childhood include hydatid disease, rheumatic fever, infectious mononucleosis and hemolytic uremic syndrome.^{12,14,15} Mechanisms of sudden death include overwhelming septic shock, cardiac arrhythmia, vascular embolization, anaphylaxis or airway obstruction (Table 1).

A classical presentation of Lemierre syndrome includes fever, neck swelling, respiratory symptoms, oropharyngeal pain and arthralgia.^{8,16} In the reported case there was evidence of an upper respiratory tract and bilateral ear infections for a number of days prior to medical evaluation. Although hospital assessment was recommended, precipitate clinical deterioration occurred a short time later with collapse and cardiorespiratory arrest.

Modern Western societies and medical practitioners have been protected against a number of the effects of bacterial agents for many decades by a sophisticated array of antibiotic drugs that are readily available and easily administered. This bulwark against infection has sometimes led to a lack of understanding of the devastating and rapid actions of many commonly occurring bacteria. In the current case earlier treatment with antibiotics would almost certainly have resulted in a different outcome, however, given the progression of disease by the time medical attention had been sought, cardiorespiratory arrest would most likely have occurred even if effective treatment could have been instituted. The fact that the child had not been taken for medical assessment earlier raises the likelihood of neglect as failure to treat middle ear infections adequately and in a timely manner is a significant issue.

Infections with *F. necrophorum* have been identified in animals for over a century and are well-recognised causes of necrotic abscesses in humans.⁷ Between 1% and 5% of anaerobic bacteremias are due to oropharyngeal infections, most often due to *F. necrophorum*.² As well as the oropharynx, primary infections may arise from the skin and subcutis, the uterus following abortion and the urinary tract. Infections may result in lung abscesses with empyema and may also follow surgery.^{17,18} There is an age-related predisposition to infection, with children tending to develop otitis media, young adults acute oropharyngeal infections and ill elderly patients having gastrointestinal or genitourinary involvement, often related to underlying cancer.^{9,19}

The infecting organisms are filamentous, nonmotile, obligate anaerobic, gram-negative bacteria that have considerable morphologic pleomorphism and that form part of the normal oropharyngeal flora.⁷ It has been suggested that there is a predisposition to Lemierre syndrome in individuals with infectious mononucleosis, possibly due to transient immunosuppression induced by the Epstein Barr virus,^{20,21} although there may be a false positive result

Table 1

Mechanisms of sudden/unexpected death in childhood due to sepsis.

Overwhelming septic shock
Cardiac arrhythmia
Electrolyte disturbance/dehydration
Vascular embolization
Anaphylaxis
Airway obstruction

in screening for heterophile antibodies in those with the syndrome.⁹ Mucosal damage, including that from either bacterial or viral pharyngitis, may predispose to infection which may also possibly result from the acquisition of a more virulent strain of organism.^{7,22} A third of individuals with Lemierre syndrome have polymicrobial bacteremia.² The classical finding of septic thrombophlebitis of the internal jugular vein^{23–26} may lead to metastatic septic emboli involving particularly the lungs with pulmonary involvement reported in up to 85% of cases.^{2,22,27} In addition, hypercoagulability has been associated with antiphospholipid antibodies and elevated factor VIII levels.²⁷ Thrombophlebitis may also involve other vessels including peritonsillar veins and the pharyngeal venous plexus, with thromboses of the lateral and cavernous sinuses.¹⁰ Other serious complications include meningitis and descending necrotizing mediastinitis, sometimes with retroperitoneal extension, associated with necrosis of infected blood vessel walls.^{3,28–31} Joints may be involved in up to 26% of cases and manifest either sterile effusions or suppurative arthritis, and there may be endocarditis.^{17,32} Jaundice may be observed, possibly caused by bacterial endotoxins. Treatment consists of early administration of antibiotics with anaerobic coverage, continued until resolution of abscesses can be demonstrated, with surgical drainage of persistent abscesses if required.³² While death is now rare, occurring in only 5% of published cases,⁷ the mortality rate in the pre-antibiotic era was as high as 90%.^{10,12} This is, however largely dependent on the age of the victim, and presence or absence of associated diseases, as elderly individuals with cancer tend to have a higher mortality rate than younger previously healthy individuals.^{9,33}

The autopsy approach to cases of possible sepsis including Lemierre syndrome involves careful examination of the exterior of the body for evidence of infection, followed by an internal examination with special dissection of any organs or tissues where suppuration is identified. Lesions and infected areas should be photographically documented. Anaerobic and aerobic blood cultures should be taken from the right atrium after sterilization with isopropyl alcohol. This is a preferable sterilizing agent to ethanol as isopropyl alcohol does not cause false positive results if the blood is also being submitted for toxicological screening for ethanol. Areas with obvious infection should also be sampled with swabs that can be sent to the microbiology laboratory in transport media. Fecal swabs and samples should both be taken if significantly fluid feces are identified. Similarly, samples of urine or cerebrospinal fluid should be aseptically taken and submitted for analysis in sterile containers. In cases of unexpected childhood death where no obvious cause is found after autopsy examination, we routinely take anaerobic and aerobic blood cultures, cerebrospinal fluid, lung and spleen swabs for bacteriology and a portion of cardiac tissue for Coxsackie

virus detection. If a specific virus is suspected, polymerase chain reaction (PCR) studies may be performed on tissue sections. Finally, once all of the results are available, a case discussion with an infectious disease physician may provide an invaluable clinical perspective and assessment of the possible significance of laboratory results (Table 2).

This case demonstrates, therefore, a rare cause of unexpected death in childhood that should be considered at autopsy if there is evidence of an oropharyngeal or ear infection with surrounding soft tissue swelling. The potential value of post-mortem microbiological testing, even several days after death, is also clearly confirmed. Given the increasing frequency of reports in the literature, Lemierre syndrome may be encountered by pathologists more often at autopsy in the future.

Conflict of Interest

None declared.

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Ethical Approval

Ethical approval is not applicable.

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Table 2
Autopsy steps in cases of suspected lethal sepsis in childhood.

1.	External examination for evidence of infection
2.	Full internal examination with <ol style="list-style-type: none"> Detailed dissection of areas of suppuration Photography
3.	Microbiological sampling to include <ol style="list-style-type: none"> Aerobic and anaerobic blood cultures Wet swabs of infected tissues or organs Samples of potentially infected fluids/material in sterile containers
4.	In cases of uncertain causes of death <ol style="list-style-type: none"> Aerobic and anaerobic blood cultures Wet swabs of lung and spleen Cerebrospinal fluid Tissue for viral studies PCR on tissue sections if indicated
5.	Discussion of results with an infectious disease physician

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